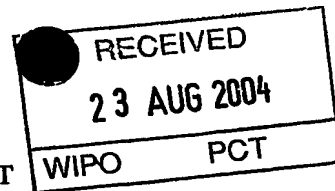


# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference <b>D6512PCT</b>	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. <b>PCT/US03/16935</b>	International filing date (day/month/year) <b>30 May 2003 (30.05.2003)</b>	Priority date (day/month/year) <b>03 June 2002 (03.06.2002)</b>
International Patent Classification (IPC) or national classification and IPC <b>IPC(7): A61B 5/055 and US Cl.: 424/9.3, 9.36, 9.364, 9.37</b>		
Applicant <b>FREDERICKSON, CHRISTOPHER</b>		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 3 sheets, including this cover sheet.  
  
☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of     sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of report with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand <b>05 January 2004 (05.01.2004)</b>	Date of completion of this report <b>05 August 2004 (05.08.2004)</b>
Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer <i>Michael G. Hartley</i> Telephone No. (703) 308-1235

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US03/16935

## I. Basis of the report

## 1. With regard to the elements of the international application:\*

- ☒ the international application as originally filed.
- ☒ the description:  
pages 1-40 as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_.
- ☒ the claims:  
pages 41-49, as originally filed  
pages NONE, as amended (together with any statement) under Article 19  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_.
- ☒ the drawings:  
pages 1 and 2, as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_.
- ☐ the sequence listing part of the description:  
pages NONE, as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_.

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.  
These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

## 3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages NONE
- ☐ the claims, Nos. NONE
- ☐ the drawings, sheets/fig NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\* Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.  
PCT/US03/16935

## V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

### 1. STATEMENT

Novelty (N)	Claims <u>4,6-8,10-12,17-19,22,24 and 26</u>	YES
	Claims <u>1-3,5,9,13-16,20,21,23,25 and 27-36</u>	NO
Inventive Step (IS)	Claims <u>NONE</u>	YES
	Claims <u>1-36</u>	NO
Industrial Applicability (IA)	Claims <u>1-36</u>	YES
	Claims <u>NONE</u>	NO

### 2. CITATIONS AND EXPLANATIONS

Claims 1-3,5,9,13-16,20,21,23,25 and 27-36 lack novelty under PCT Article 33(2) as being anticipated by Sherry (US 5,188,816). Sherry discloses a method of MRI comprising administering an MRI agent, acquiring image signal, wherein the intensity is sensitive to the relaxation times and generating an image map by correlating with image pixel on the map, see columns 1 and 2 and columns 9-10. Sherry discloses that various contrast agents may be employed, such as, various chelates, see columns 3-4. The various steps in the claims are required steps of measuring shifts in NMR/MRI (chemical shift imaging) as disclosed by Sherry.

Claims 1-36 lack an inventive step under PCT Article 33(3) as being obvious over Sherry (US in view of Ramasamy (US 5,834,466) and Zamora (US 5,690,905).

Sherry teaches methods of MRI wherein the intensity is sensitive to the relaxation times, as set forth above, but fails to disclose the use of the same fluorinated (F-19) chelates and/or targeting chelates, as claimed.

Ramasamy teaches that fluorinated (F-19) chelates, as claimed, are especially useful in NMR?MRI monitoring methods, see column 12.

Zamora teaches that various chelates, which are useful as contrast agents, should include a targeting agent to provide the advantage of site specificity to the contrast agents, see column 2.

It would have been obvious to one of ordinary skill in the art to employ either F-19 chelates and/or targeting chelates (as claimed) in the methods disclosed by Sherry because the use of the F-19 chelates and/or targeted chelates, as claimed, are known to provide the advantages of monitoring tissues by MRI and providing targeted contrast agents, as shown by Ramasamy and Zamora in related MRI methods.

Claims 4,6-8,10-12,17-19,22,24 and 26 the criteria set out in PCT Article 33(2), because the prior art does not disclose methods of chemical shift MRI as claimed using the specific F-19 and/or targeted chelates as claimed.

Claims 1-36 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

Applicant's arguments filed on 07 July 2004 have been fully considered, but are not found persuasive.

Applicant asserts that Sherry neither teaches the use of the chelators for in vivo mapping of concentration of a taruget metal ion nor teaches every step in claim 1.

This is not found persuasive because Sherry specifically discloses that the chelators are used to assess the concentration of metal ions in vivo, see column 2. Also, the NMR scanning in chemical shift imaging to obtain an image, as disclosed by Sherry, would necessitate the acquisition, generating and correlating steps in claim 1, as these steps are part of such scanning to provide the image. Applicant asserts that the disadvantages suggested by Sherry would discourage the skilled artisan from using F-19 chelates or targeted chelates.

This is not found persuasive because Sherry only teaches an improvement over a specific F-19 chelate, but does not specifically teach away from using F-19 for detection. Sherry provides no teaching away from using F-19 for in vivo imaging. Ramasamy also teaches that F-19 chelates are preferred for NMR/MRI. The use of targeting agents to provide the advantage of site-specificity are well known as shown by Zamora.